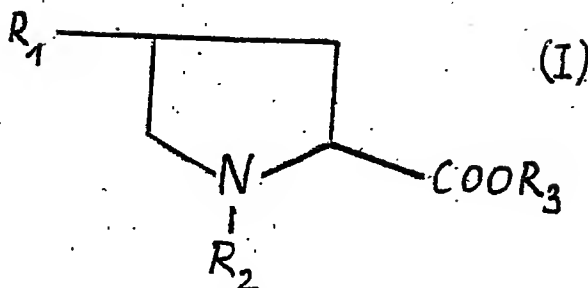


TRANSLATION OF ANNEX OF THE INTERNATIONAL PRELIMINARY EXAMINATION
REPORT (IPER) FOR PCT/DE2003/004211

Main request

Amended claims:

1. A compound of general formula (I),



wherein

R_1 is a hydroxy, aryl or amino acid group,

R_2 is hydrogen, an alkyl (C_1-C_4), a substituted alkyl (C_1-C_4) group, a dialkyl (C_1-C_4), a cyclohexyl, a phenyl or diphenyl group,

R_3 is an alkyl (C_2-C_5) group,

and/or salts thereof,

with the proviso that, if R_1 is a hydroxy group, R_2 is not a methyl group,

said compound being selected from the group comprising 4-hydroxy-1,1-dimethylproline ethyl ester iodide, 4-hydroxyproline isobutyl ester, 4-hydroxy-1,1-dimethylproline isobutyl ester iodide, 4-hydroxy-1-cyclohexylproline isobutyl ester, 4-hydroxy-1-diphenylmethylproline isobutyl ester hydrobromide, 4-hydroxy-1-methylproline ethyl ester, 4-hydroxy-1-methylproline isobutyl ester and/or 1-methyl-4-phenylaminocarbonyloxypyrrolidine isobutyl ester, and, if R_1 is a hydroxy group, said compounds may have a methyl group in position R_2 .

2. A pharmaceutical agent comprising a compound according to the preceding claim, optionally together with conventional auxiliaries, preferably pharmaceutically acceptable carriers, adjuvants and/or vehicles.
3. The pharmaceutical agent according to the preceding claim, characterized in that the carriers are selected from the group comprising fillers, diluents, binders, humectants, disintegrants, dissolution retarders, absorption enhancers, wetting agents, adsorbents and/or lubricants.
4. The pharmaceutical agent according to any of claims 2 or 3, characterized in that the carriers are liposomes, siosomes and/or niosomes.
5. The pharmaceutical agent according to any of claims 2 to 4, characterized in that the agent additionally comprises a chemotherapeutic agent.
6. The pharmaceutical agent according to the preceding claim, characterized in that the chemotherapeutic agent is selected from the group comprising oxoplatin, cis-oxoplatin, taxol, gemcitabine, vinorelbine, paclitaxel, cyclosporin and/or a combination thereof.
7. The pharmaceutical agent according to any of claims 2 to 6, characterized in that

it also comprises one or more additional agents from the group of antiviral, antimycotic, antibacterial and/or immunostimulatory agents.

8. Use of the compound according to claim 1 and/or of the pharmaceutical agent according to any of claims 2 to 7 in the production of a drug for the diagnosis, prophylaxis, follow-up, therapy, and/or aftercare of diseases associated with cell growth, cell differentiation and/or cell division, said disease being a tumor.
9. Use of 4-hydroxyproline ethyl ester, 4-hydroxy-1,1-dimethylproline ethyl ester iodide, 4-hydroxyproline isobutyl ester, 4-hydroxy-1,1-dimethylproline isobutyl ester iodide, 4-hydroxy-1-cyclohexylproline isobutyl ester, 4-hydroxy-1-diphenylmethylproline isobutyl ester hydrobromide, 4-hydroxy-1-methylproline, 4-hydroxy-1-methylproline ethyl ester, 4-hydroxy-1-methylproline isobutyl ester, 1-methyl-4-phenylaminocarbonyloxyproline, 1-methyl-4-phenylaminocarbonyloxyproline isobutyl ester, (R)-(+)- α,α -diphenyl-2-pyrrolidinemethanol and/or (S)-(-)- α,α -diphenyl-2-pyrrolidinemethanol and/or derivatives, metabolites, enantiomers and/or isomers thereof in the diagnosis, prophylaxis, follow-up, therapy, and/or aftercare of diseases associated with cell growth, cell differentiation and/or cell division, said disease being a tumor.
10. The use according to preceding claim, characterized in that the tumor diseases are selected from the group of neoplastic tumors, inflammatory tumors, abscesses, effusions and/or edemas.

11. The use according to the preceding claim,
characterized in that
the tumor is a solid tumor or a leukemia.
12. The use according to the preceding claim,
characterized in that
the solid tumor is a tumor of the urogenital tract and/or
gastrointestinal tract.
13. The use according to any of claims 8 to 12,
characterized in that
the tumor is a colon carcinoma, stomach carcinoma, pan-
creas carcinoma, small intestine carcinoma, ovarian carci-
noma, cervical carcinoma, lung carcinoma, prostate carci-
noma, mammary carcinoma, renal cell carcinoma, a brain tu-
mor, head-throat tumor, liver carcinoma, and/or a metas-
tase of the above tumors.
14. The use according to any of claims 8 to 13,
characterized in that
the solid tumor is a mammary, bronchial, colorectal,
and/or prostate carcinoma and/or a metastase of the above
tumors.
15. The use according to any of claims 8 to 14,
characterized in that
the tumor of the urogenital tract is a bladder carcinoma
and/or a metastase of such tumors.
16. The use according to any of claims 8 to 15,
characterized in that
said follow-up is monitoring the effectiveness of an anti-
tumor treatment.

17. The use according to any of claims 8 to 16,
characterized in that
at least one compound according to claim 1 and/or a pharmaceutical agent according to any of claims 2 to 7 are employed in the prophylaxis, prevention, diagnosis, attenuation, therapy, follow-up and/or aftercare of metastasizing, invasion, infiltration, tumor growth and/or angiogenesis.
18. The use according to any of claims 8 to 17,
characterized in that
said follow-up is monitoring the effectiveness of an anti-tumor treatment.
19. The use according to any of claims 8 to 18,
characterized in that
at least one compound according to claim 1 and/or a pharmaceutical agent according to any of claims 2 to 7 are employed in a combined therapy.
20. The use according to the preceding claim,
characterized in that
said combined therapy comprises a chemotherapy, a treatment with cytostatic agents and/or a radiotherapy.
21. The use according to the preceding claim,
characterized in that
the combined therapy comprises an adjuvant, biologically specified form of therapy.
22. The use according to the preceding claim,
characterized in that

said form of therapy is an immune therapy.

23. The use according to any of claims 8 to 22 to increase the sensitivity of tumor cells to cytostatic agents and/or radiation.
24. The use according to any of claims 8 to 23 for inhibiting the viability, the proliferation rate of cells in order to induce apoptosis and/or cell cycle arrest.
25. The use according to any of claims 8 to 24, characterized in that
at least one compound according to claim 1 and/or a pharmaceutical agent according to any of claims 2 to 7 are prepared as gel, poudrage, powder, tablet, sustained-release tablet, premix, emulsion, brew-up formulation, drops, concentrate, granulate, syrup, pellet, bolus, capsule, aerosol, spray and/or inhalant and/or inhalant and applied in this form.
26. The use according to the preceding claim, characterized in that
at least one compound according to claim 1 and/or a pharmaceutical agent according to any of claims 2 to 7 are present in a preparation at a concentration of from 0.1 to 99.5, preferably from 0.5 to 95.0, and more preferably from 20.0 to 80.0 weight percent.
27. The use according to the preceding claim, characterized in that
the preparation is employed orally, subcutaneously, intravenously, intramuscularly, intraperitoneally and/or topically.

28. The use according to any of claims 8 to 27,
characterized in that
at least one compound according to claim 1 and/or a pharmaceutical agent according to any of claims 2 to 7 are employed in overall amounts of more than 0.1 g per kg body weight per 24 hours.
29. The use according to any of claims 8 to 28,
characterized in that
at least one compound according to claim 1 and/or a pharmaceutical agent according to any of claims 2 to 7 are employed in overall amounts of 0.05 to 500 g per kg, preferably 5 to 100 g per kg body weight per 24 hours.
30. A method for the treatment of a tumor disease,
characterized in that
an organism is contacted with an effective amount of a compound according to claim 1 and/or a pharmaceutical agent according to any of claims 2 to 7.
31. Use of the compound according to claim 1 and/or the pharmaceutical agent according to any of claims 2 to 7 for inhibiting collagen IV and/or glutathione S transferase (GST).
32. A method for the preparation of a compound according to claim 1,
characterized in that
1-methyl-4-phenylaminocarbonyloxypyrrolidine ethyl ester is obtained by reacting 4-hydroxy-1-methylpyrrolidine ethyl ester and phenyl isocyanate in acetonitrile.

33. A method for the preparation of a compound according to claim 1,
characterized in that
1-methyl-4-phenylaminocarbonyloxyproline isobutyl ester is obtained by reacting 4-hydroxy-1-methylproline isobutyl ester and phenyl isocyanate in acetonitrile.
34. A method for the preparation of a compound according to claim 1,
characterized in that
4-hydroxy-1-methylproline is obtained by reacting 4-hydroxyproline in formalin with Pd/C in a hydrogenation apparatus.
35. A method for the preparation of a compound according to claim 1,
characterized in that
4-hydroxy-1-methylproline ethyl ester is obtained by reacting 4-hydroxyproline ethyl ester and formalin in ethanol.
36. A method for the preparation of a compound according to claim 1,
characterized in that
4-hydroxy-1-methylproline isobutyl ester is obtained by reacting formalin, Pd/C and ethanol and 4-hydroxyproline isobutyl ester.
37. A method for the preparation of a compound according to claim 1,
characterized in that

4-hydroxy-1-methylproline isobutyl ester is obtained by reacting formalin and 4-hydroxyproline isobutyl ester in the presence of Pd/C in ethanol.

38. A method for the preparation of a compound according to claim 1,
characterized in that
cis-4-hydroxy-L-proline ethyl ester is obtained by contacting 4-hydroxyproline with HCl in ethanol.
39. A method for the preparation of a compound according to claim 1,
characterized in that
cis-4-hydroxy-L-proline isobutyl ester is obtained by reacting 4-hydroxyproline in isobutanol.
40. A method for the preparation of a compound according to claim 1,
characterized in that
4-hydroxy-1,1-dimethylproline ethyl ester iodide is obtained by reacting hydroxyproline ethyl ester in acetonitrile, methyl iodide and triethylamine.
41. A method for the preparation of a compound according to claim 1,
characterized in that
4-hydroxy-1,1-dimethylproline isobutyl ester iodide is obtained by reacting 4-hydroxyproline isobutyl ester and methyl iodide in triethylamine and acetonitrile.
42. A method for the preparation of a compound according to claim 1,
characterized in that

4-hydroxy-1-alkylproline ester bromide is obtained by suspending 4-hydroxyproline ester in acetonitrile and contacting with the corresponding alkyl bromide in the presence of ether.

43. A method for the preparation of a compound according to claim 1,
characterized in that
4-hydroxy-1-cyclohexylproline isobutyl ester is obtained by dissolving the corresponding hydrobromide in chloroform and contacting with gaseous ammonia.
44. A method for the preparation of a compound according to claim 1,
characterized in that
4-hydroxy-1-diphenylmethylproline isobutyl ester hydrobromide is obtained by contacting 4-hydroxyproline isobutyl ester, methyl iodide, triethylamine in acetonitrile.
45. A kit comprising at least one compound according to claim 1 and/or a pharmaceutical agent according to any of claims 2 to 7, optionally together with information for combining the contents of the kit.
46. Use of the kit according to the preceding claim in the prophylaxis or therapy of tumor diseases.

